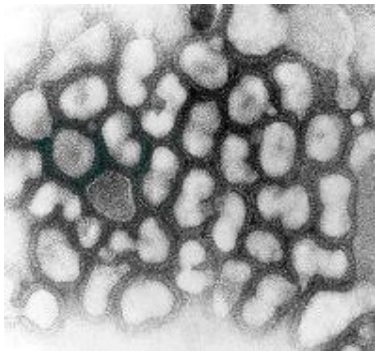
Surveillance for Avian Influenza A (H5N1) in California:

UPDATED September 25, 2006

On January 15, 2004, the California Department of Health Services (CDHS) issued recommendations for enhanced surveillance for avian influenza A (H5N1). This website provides information on background, current recommendations for enhanced surveillance in California, diagnostic testing, and management, including infection control guidelines, for influenza A (H5N1) cases.



Avian influenza outbreaks in poultry and other animals

In December 2003 - February 2004, widespread outbreaks of highly pathogenic influenza A (H5N1) in poultry were reported in Cambodia, China, Taiwan, Hong Kong SAR, Malaysia, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam. The spread of a highly pathogenic form of avian influenza in poultry to so many countries in such a short period of time was unprecedented. Since those initial reports, avian influenza A (H5N1) outbreaks in both domestic poultry and wild birds, with associated human cases, continue to be reported in a growing number of countries. The likely vector of spread is migratory wild birds, which may harbor many strains of avian influenza and remain healthy-appearing. Over the summer of 2005 the influenza A (H5N1) virus was identified in wild birds in Mongolia. Last spring 2005 the virus killed several thousand birds in the Qinghai Lake wildlife refuge in north-central China, which borders Mongolia on the south. This preceded the identification several months later of influenza A (H5N1) in domestic poultry in Siberian Russia and Kazakhstan.

Since late 2005, avian influenza (H5N1) infection has continued to spread rapidly to other regions of the world. In October 2005, the World Organization for Animal Health (OIE) confirmed the presence of highly pathogenic avian influenza H5N1 in domestic poultry in several countries in Central and Eastern Europe, accompanied by reports of large poultry outbreaks and associated human cases in Turkey. In the first few months of 2006, avian influenza (H5N1) infection has been confirmed in both poultry and wild bird populations in Western Europe, the Middle East, Northern Africa, SubSaharan

Africa, Pakistan and India. The situation in these recently affected countries varies greatly, ranging from widespread poultry outbreaks in some to detection of the virus in only a small number of wild birds in others. Accurate assessment of the extent of H5N1 outbreaks in many of these countries is hampered by limited resources and infrastructure to perform surveillance, including laboratory confirmation.

To date, more than 150 million domestic poultry have either died from the disease or have been culled (killed) in efforts to contain the outbreaks. While Japan and South Korea appear to have instituted effective control measures in their outbreaks, which were primarily limited to commercial poultry farms, outbreaks may recur at any time. The remaining areas are considered to have either active avian influenza A (H5N1) outbreaks or sporadic surveillance and control measures making them at high risk for avian influenza outbreaks. For an updated listing of countries with H5N1 poultry outbreaks, visit the World Organization of Animal Health (OIE) webpage on Avian Influenza (Type H5) in Animals and click on “GRAPH” at the top of the page.

Graph - Outbreaks of Highly Pathogenic Avian Influenza (Type H5) (as of 09/04/06)



Besides domestic poultry (e.g. chickens, ducks, turkeys, geese and quail), influenza A (H5N1) has been confirmed in other animals including pigs and wild and domestic cats. Experimental infection of housecats in the Netherlands and isolation of H5N1 viruses from infected tigers and leopards in Thailand suggest that cats can both host and transmit the infection. The presence of the virus in pigs is of concern because pigs can be co-infected with both avian influenza and human influenza viruses and could serve as a “mixing vehicle.” If a pig were infected with both viruses at the same time, the viruses could reassort and produce a new virus that might then be able to infect humans and spread from person to person, but it would have surface proteins (hemagglutinin and/or neuraminidase) not previously seen in influenza viruses that infect humans. More worrisome, ducks infected with H5N1 can shed virus for longer periods of time without showing any symptoms of illness. These findings have serious implications for the expanding role of ducks, wild birds, and other unrecognized animal vectors to transmit disease to human populations. It also highlights how difficult it is to completely eliminate H5N1 avian influenza virus in these wild animal populations, and the region as a whole.

Avian influenza outbreaks in humans

Despite the rapid spread of avian influenza (H5N1) worldwide, all evidence to date indicates that the H5N1 virus does not spread easily from birds to infect humans. The risk remains highest in persons who reside in countries with widespread outbreaks in poultry, and who have had direct contact with infected poultry, or surfaces and objects contaminated by their droppings (e.g. persons exposed during slaughter, defeathering, butchering, and preparation of poultry for cooking). There is no evidence that properly cooked poultry or poultry products can be a source of infection.

As the virus spreads, WHO continues to report increasing numbers of human avian influenza (H5N1) cases. In 2006, human cases have been reported in Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Thailand, and Turkey. The first confirmed case in Thailand was reported in July 2006. The table below lists the current WHO count of laboratory confirmed human influenza A (H5N1) cases:

Country	2003		2004		2005		2006		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	8	5
Cambodia	0	0	0	0	4	4	2	2	6	6
China	1	1	0	0	8	5	12	8	21	14
Djibouti	0	0	0	0	0	0	1	0	1	0
Egypt	0	0	0	0	0	0	14	6	14	6
Indonesia	0	0	0	0	19	12	48	39	67	51
Iraq	0	0	0	0	0	0	3	2	3	2
Thailand	0	0	17	12	5	2	2	2	24	16
Turkey	0	0	0	0	0	0	12	4	12	4
Viet Nam	3	3	29	20	61	19	0	0	93	42
Total	4	4	46	32	97	42	102	68	249	146

Table Updated September25, 2006

Notes

- Overall case fatality rate of 59%
- WHO reports only laboratory-confirmed cases
- Total number of cases includes number of deaths
- For more information please see the WHO Avian Influenza website.

Most cases of H5N1 infection in humans are thought to have occurred from direct contact with infected poultry. Therefore, travelers to affected areas are advised to avoid contact with live, well-appearing, sick, or dead poultry and any surfaces that may have been contaminated by poultry or their feces or secretions. Transmission of H5N1 viruses to two persons through consumption of uncooked duck blood may also have occurred in Vietnam in 2005. Therefore, consumption of uncooked poultry or poultry products, including blood, should be avoided. More detailed recommendations for travelers to affected countries can be found in the CDC Notice to Travelers about Avian Influenza A (H5N1).

H5N1 infections in humans can cause serious disease and death. Frequent clinical signs and symptoms include fever, shortness of breath, cough and diarrhea. These symptoms can progress rapidly to development of severe pneumonia and multi-organ failure. No vaccine to protect humans against H5N1 infection is currently available, but an inactivated human H5N1 vaccine is undergoing human clinical trials in the United States. The H5N1 viruses currently infecting birds and some humans in Asia are resistant to amantadine and rimantadine, two antiviral medications commonly used for influenza. The H5N1 viruses are susceptible to the antiviral medications oseltamavir and zanamavir, although the effectiveness of these drugs when used for treatment of H5N1 virus infection is unknown.

Reports of unusual clinical presentations and asymptomatic infections:

Unusual clinical presentations have been reported. One case of H5N1 infection described in Vietnam was a four-year-old boy presented with symptoms of severe diarrhea, followed by seizures, coma and death. The patient's nine-year-old sister had died from a similar syndrome two weeks earlier. In both siblings, the clinical diagnosis was acute encephalitis with neither patient presenting with respiratory symptoms.

In addition, cases of asymptomatic H5N1 infection have been reported. These are not unexpected, and were observed when the virus first jumped to humans in Hong Kong in 1997. Undetected cases might imply that infections with H5N1 influenza may be more common than previously thought, suggesting that the overall case fatality rate may not be as high as previously suggested. It also raises the question of whether mild and/or asymptomatic cases of avian flu allow the virus more opportunities to mix, or "re-assort," with human-adapted flu viruses. This genetic mixing increases the likelihood of generating a virus that is able to efficiently spread from person to person. As more data become available, the WHO will be assessing the number of asymptomatic and undetected avian influenza cases in Asia, and their implications for triggering a flu pandemic.

Isolated clusters of human-to-human transmission:

Almost all human avian influenza cases appear to have occurred because of bird-to-human transmission. However, an isolated cluster of probable limited human-to-human transmission of influenza A (H5N1) virus has also been observed. This instance of probable person-to-person transmission was associated with close contact between an ill child and her mother and is thought to have occurred in Thailand in September 2004. So far, no sustained human-to-human transmission of influenza A (H5N1) has been identified, and no influenza A (H5N1) viruses containing both human and avian influenza virus genes have been detected.

Surveillance Guidelines for Avian Influenza A (H5N1) Human Cases in California:

California is in a key location to be one of the first states possibly affected given its many ports of entry and frequent traffic from Asia. Surveillance for influenza is important to rapidly identify the importation of pandemic strains into California.

The California Department of Health Services (CDHS) recommendations for avian influenza A (H5N1) remain at the enhanced level established in February 2004. Enhanced surveillance efforts by clinicians, hospitals, and local and state health departments will help identify patients at increased risk for influenza A

(H5N1) infection. **All health care providers should consult with their local health department when assessing a suspect case** for advice on diagnostic testing and specimen submission using the following guidelines.

CDHS Surveillance Criteria for Influenza A (H5N1) Infection:

Testing for avian influenza A (H5N1) is RECOMMENDED:

A patient who has an illness that requires **hospitalization** or is **fatal**; **AND** has a documented fever >38°C (100.4°F); **AND** has radiographically- confirmed pneumonia, acute respiratory distress syndrome (ARDS) or other respiratory illness with no alternate diagnosis established; **AND** has at least **one** of the following exposures within 10 days of symptom onset:

A. Travel to an area with documented avian (H5N1) influenza[1] in poultry[2], wild birds and/or humans with at least one of the following:

- Direct contact with (e.g. touching) sick or dead domestic poultry[2]; OR
- Direct contact with surfaces contaminated with poultry[2] feces; OR
- Consumption of raw or incompletely cooked poultry[2] or poultry[2] products; OR
- Direct contact with sick or dead wild birds suspected or confirmed to have influenza H5N1; OR
- Close contact (within 1 meter or 3 feet) of a person who was hospitalized or died due to unexplained respiratory illness.

OR

B. Close contact (within 1 meter) of an ill patient who was confirmed or suspected to have H5N1;

OR

C. Worked with live influenza H5N1 virus in a laboratory.

TESTING ON A CASE-BY-CASE BASIS IN CONSULTATION WITH THE LOCAL HEALTH DEPT SHOULD BE CONSIDERED:

- o A hospitalized or ambulatory patient with mild or atypical disease (e.g., diarrhea or encephalitis without respiratory disease) with one of the above exposures (A, B or C)

OR

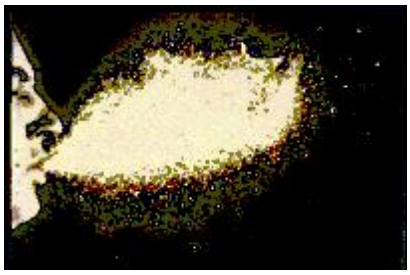
- o A patient with severe or fatal respiratory disease whose epidemiological information is uncertain, unavailable or suspicious, but does not meet criteria listed above (e.g. returned traveler from an affected country with unclear exposure, or with contact with well-appearing poultry[2])

1. For a list of affected countries, visit the Web site of the World Organization of Animal Health (OIE) and click on "GRAPH" at the top of the page)

2. The definition of poultry is: domestic fowls, such as chickens, turkeys, ducks, or geese, raised for meat or eggs.

For any cases meeting the above criteria, contact your local health department. Local health departments should fill out the CDHS Screening Form for Suspect Avian (H5N1) Influenza and report any suspect or laboratory-confirmed case to the CDHS VRDL or Duty Officer of the Day immediately.

Infection Control Precautions for Avian Influenza A (H5N1)



All patients presenting to a health-care setting with fever and respiratory symptoms should be questioned regarding their recent travel history and managed using CDC Respiratory Hygiene and Cough Etiquette. In addition,

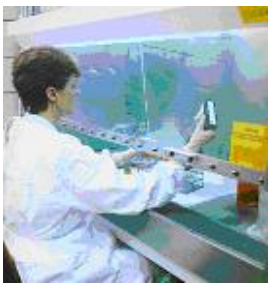
- For suspect avian influenza (H5N1) patients who are sufficiently ill to be hospitalized, **airborne, droplet and contact precautions** are recommended. Hospitalized patients should be managed with appropriate isolation precautions for 14 days after onset of symptoms unless an alternative diagnosis is established or infection with influenza A (H5N1) has been excluded.

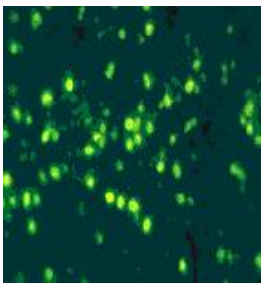
- For suspect avian influenza (H5N1) patients who can be managed at home (e.g., patients managed as outpatients or hospitalized patients discharged before 14 days), **modified droplet and contact precautions** are recommended.

For more detailed infection control guidelines, please review the:
Avian Influenza A (H5N1) Infection Control Recommendations for Suspect Cases

- Note: CDC is in the process of revising its interim guidance for infection control precautions for influenza A (H5N1). When those revised guidelines are available, CDHS will update this document to reflect any changes.

Testing for Avian Influenza A (H5N1)





Diagnostic testing is recommended for suspect cases who meet the CDHS Surveillance Criteria for Influenza A (H5N1) infection. Polymerase chain reaction (PCR) for influenza A and B, including subtyping, is available at certain local public health laboratories in California and the CDHS Viral & Rickettsial Disease Laboratory (VRDL). In all situations, a portion of specimens in suspect H5N1 cases should be forwarded to VRDL for concurrent testing as soon as possible.

Questions regarding submission of specimens on suspect cases of avian influenza A (H5N1), and where specimens should be submitted, should be directed to the local health department.

Rapid antigen testing or PCR for influenza can be performed under BSL-2 conditions. However, commercial rapid influenza antigen testing in the evaluation of suspected influenza A (H5N1) cases should be interpreted with caution. The sensitivity and specificity of rapid antigen testing can vary depending on the timing and type of specimen obtained, and a negative result does not exclude a diagnosis of avian influenza A (H5N1). In addition, a positive result does not distinguish between seasonal and avian influenza A viruses. Therefore, if a patient tests negative for influenza by rapid antigen testing but meets the CDHS Surveillance Criteria for Influenza A (H5N1) Infection, specimens should be sent for further characterization (including PCR and subtyping) to the local public health laboratories or VRDL.

Highly pathogenic avian influenza A (H5N1) is classified as a select agent and isolation for the virus can only be done under Biosafety Level (BSL) 3+ laboratory conditions. Laboratories working on these viruses must be certified by the U.S. Department of Agriculture. **Therefore, viral culture on specimens from patients meeting the above criteria should NOT be attempted by hospital or private laboratories, or by local public health laboratories.** Laboratories should refer to the CDHS Laboratory Biosafety Guidelines for Handling and Processing Specimens or Isolates of Influenza A (H5N1) Strains for further information.

For submission of specimens, the CDHS Guidelines for Collecting and Shipping Specimens for Influenza A (H5N1) Diagnostics should be used.

To improve diagnostic sensitivity, testing should be performed on multiple sample types. Some studies have demonstrated the need for multiple samples collected over several days for optimal H5 detection sensitivity. Given that most human cases have presented with lower respiratory tract infections, the collection of only an upper respiratory specimen, particularly single nasopharyngeal or nasal swabs, is NOT recommended.

MINIMUM SPECIMEN REQUIREMENTS INCLUDE THE FOLLOWING:

1) An oropharyngeal swab collected in 3 cc viral transport media (VTM); AND
2) A nasopharyngeal swab OR wash OR aspirate collected in 3 cc viral transport media (VTM)*; AND
3) Any specimen(s) from the lower respiratory tract (e.g., sputum, bronchoalveolar lavage, tracheal aspirate or pleural fluid tap)*.

* Oropharyngeal swabs may have better yield than nasopharyngeal specimens. While both types of specimens should be collected, an oropharyngeal swab should be performed preferentially if only one sample can be taken.

** In outpatient settings, it may be difficult to obtain samples from the lower respiratory tract in children. In these instances, two specimens from the upper respiratory tract (e.g. a nasopharyngeal wash and a throat swab) are acceptable.

After review with the local health department, any requests for diagnostic testing at VRDL must be accompanied by the VRDL Specimen Submittal Form. Local health departments may call David Cottam at the CDHS VRDL at (510) 307-8585 for further assistance.

INFECTION CONTROL PRECAUTIONS DURING SPECIMEN COLLECTION:
Infection control precautions during specimen collection should include the use of gloves, gown, goggles or face shield, and a fit-tested respirator with an N-95 or higher-rated filter. A loose-fitting powered air-purifying respirator (PAPR) may be used if fit-testing is not possible (for example, if the person has a beard). For detailed guidance, please see the CDHS Infection Control Recommendations for Suspect Cases of Avian Influenza A (H5N1).

ANY SUSPECT OR LABORATORY-CONFIRMED CASES SHOULD BE REPORTED TO THE LOCAL HEALTH DEPARTMENT AND CDHS IMMEDIATELY.

Additional Avian Influenza A (H5N1) Information:

- For information about reported outbreaks of avian influenza A (H5N1) among poultry, see the web site of the World Organization of Animal Health (OIE).

  * As the list of affected countries continues to change, the most up to date information can be found on the OIE Avian Influenza in Animals website.

- For information about human H5N1 cases, see the WHO website.

  * For additional information on the current H5N1 situation in Asia please refer to the World Health Organization (WHO) Avian Influenza website, or the Centers for Disease Control and Prevention (CDC) Avian Influenza website.

- For clinical information about human H5N1 cases, see:

  * CDC. Cases of influenza A (H5N1) – Thailand , 2004. MMWR 2004;53:100-103.

  * Hien TT, Liem AT, Dung NT, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. New England Journal of Medicine 2004;350:1179-1188

- For information for travelers to avian influenza A (H5N1) affected areas, see the CDC Notice to Travelers about Avian Influenza A (H5N1).

- For more information about avian influenza, please see the University of Minnesota Center for Infectious Disease Research and Policy (CIDRAP) Avian Influenza webpage.